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NEWS 18 SEP 11 CA/CAplus enhanced with more pre-1907 records
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NEWS 21 SEP 25 CAS REGISTRY(SM) no longer includes Concord 3D coordinates
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NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

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=> s (methotrexate or methotrexate(w)triglutamate) and
(prostate(w)specific(w)membrane(w)antigen or PMSA)

L1 33 (METHOTREXATE OR METHOTREXATE(W) TRIGLUTAMATE) AND (PROSTATE(W)
SPECIFIC(W) MEMBRANE(W) ANTIGEN OR PMSA)

=> dup rem

ENTER L# LIST OR (END):11

PROCESSING COMPLETED FOR L1

L2 24 DUP REM L1 (9 DUPLICATES REMOVED)

=> dis ibib abs l2 10-24

L2 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:182244 CAPLUS

DOCUMENT NUMBER: 140:223261

TITLE: Polymeric delivery systems

INVENTOR(S): Griffiths, Gary L.; Goldenberg, David M.; Hansen, Hans J.

PATENT ASSIGNEE(S): Immunomedics, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S.
Ser. No. 209,592.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004043030	A1	20040304	US 2003-456580	20030609
US 2003026764	A1	20030206	US 2002-209592	20020731
CA 2455856	AA	20030213	CA 2002-2455856	20020731
EP 1411987	A2	20040428	EP 2002-749088	20020731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005501052	T2	20050113	JP 2003-516572	20020731
PRIORITY APPLN. INFO.:			US 2001-308605P	P 20010731
			US 2002-209592	A2 20020731
			WO 2002-GB3494	W 20020731

AB The present invention relates to a method of targeting an agent towards a targeting site in a tissue comprising administering a multi-specific antibody or antibody fragment comprising a targeting arm and a capture arm that binds to a polymer conjugate, and administering a polymer conjugate

to the tissue. The present invention also relates to a kit for targeting a target site within a comprising a multi-specific antibody or antibody fragment comprising a targeting arm and a capture arm that binds to a polymer conjugate, and a polymer conjugate.

L2 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:141669 CAPLUS
DOCUMENT NUMBER: 140:216171
TITLE: Anti-PSMA antibodies and PSMA multimers for diagnosis, prognosis and therapy of prostatic or non-prostatic cancers
INVENTOR(S): Maddon, Paul J.; Donovan, Gerald P.; Olson, William C.; Schulke, Norbert; Gardner, Jason; Ma, Dangshe
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 151 pp., Cont.-in-part of Appl. No. PCT/US02/33944.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004033229	A1	20040219	US 2003-395894	20030321
WO 2003034903	A2	20030501	WO 2002-US33944	20021023
WO 2003034903	A3	20031030		
WO 2003034903	B1	20040513		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004161776	A1	20040819	US 2003-695667	20031027
US 2005215472	A1	20050929	US 2004-976352	20041027
PRIORITY APPLN. INFO.:			US 2001-335215P	P 20011023
			US 2002-362747P	P 20020307
			US 2002-412618P	P 20020920
			WO 2002-US33944	A2 20021023
			US 2003-395894	A2 20030321
			US 2003-695667	A2 20031027

AB The invention includes antibodies or antigen-binding fragments thereof which bind specifically to conformational epitopes on the extracellular domain of prostate specific membrane antigen (PSMA), compns. containing one or a combination of such antibodies or antigen-binding fragments thereof, hybridoma cell lines that produce the antibodies, and methods of using the antibodies or antigen-binding fragments thereof for cancer diagnosis and treatment. The invention also includes oligomeric forms of PSMA proteins, compns. comprising the multimers, and antibodies that selectively bind to the multimers.

L2 ANSWER 12 OF 24 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005428234 EMBASE
TITLE: Targeting prostate-specific membrane antigen in cancer therapy: Can molecular medicine be brought to the surface?.
AUTHOR: Leach F.

CORPORATE SOURCE: F. Leach, Scott Department of Urology, Baylor College of Medicine, 6560 Fannin, Houston, TX 77030, United States.
fleach@bcm.tmc.edu

SOURCE: Cancer Biology and Therapy, (2004) Vol. 3, No. 6, pp. 559-560.

Refs: 12

ISSN: 1538-4047

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer

028 Urology and Nephrology

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 27 Oct 2005

Last Updated on STN: 27 Oct 2005

AB Systemic chemotherapy can be associated with significant morbidity as a result of non-specific side effects and drug toxicity. A major advance in cancer therapy is the ability to target specific molecules and pathways due to increased knowledge of gene expression and biochemical function. In this issue of Cancer Biology & Therapy, a targeted approach to prostate cancer chemotherapy is explored using the inherent enzymatic activity of prostate-specific membrane antigen (PSMA) and peptide conjugated methotrexate. Substrate specificity and specific activity were determined using soluble PSMA while selective drug toxicity was determined using clonal inhibition of PSMA+ and PSMA- cancer cell lines. Peptide conjugates linked to methotrexate were identified with enhanced selective clonal inhibition in the presence of PSMA. Despite these promising results, multiple variables affecting clinical feasibility such as substrate stability and non-PSMA dependent drug uptake will require careful consideration before PSMA is ready for prime time as a selective chemotherapeutic target. .COPYRGT.2004 Landes Bioscience.

L2 ANSWER 13 OF 24 MEDLINE on STN

DUPLICATE 2

ACCESSION NUMBER: 2004418666 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15044850

TITLE: Use of methotrexate-based peptide substrates to characterize the substrate specificity of prostate-specific membrane antigen (PSMA).

AUTHOR: Mhaka Annastasia; Gady Alyssa M; Rosen D Marc; Lo Kin-Ming; Gillies Steven D; Denmeade Samuel R

CORPORATE SOURCE: The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, The Johns Hopkins School of Medicine, Baltimore, Maryland, USA.

SOURCE: Cancer biology & therapy, (2004 Jun) Vol. 3, No. 6, pp. 551-8. Electronic Publication: 2004-06-10. Journal code: 101137842. ISSN: 1538-4047.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200505

ENTRY DATE: Entered STN: 25 Aug 2004

Last Updated on STN: 20 May 2005

Entered Medline: 19 May 2005

AB Prostate-Specific Membrane Antigen (PSMA) is a glutamate carboxypeptidase II that is highly expressed by both normal and malignant prostate epithelial cells and by the neovasculature of many tumor types but is not expressed by endothelial cells in normal tissue. PSMA possesses the hydrolytic properties of an N-acetylated alpha-linked acidic dipeptidase (NAALADase) and also functions as a pteroyl poly-gamma-glutamyl carboxypeptidase (i.e., folate hydrolase).

Therefore, PSMA can be targeted for activation of peptide-based prodrugs within the extracellular fluid of prostate cancers. In this study, methotrexate-based peptide analogs were evaluated to identify PSMA selective substrates that are also stable to nonspecific hydrolysis in human and mouse plasma. These methotrexate analogs were also characterized for in vitro toxicity against PSMA and nonPSMA producing human cancer cell lines. Analogs containing gamma-linked glutamate residues were most efficiently hydrolyzed by PSMA, but were unstable in plasma. Analogs containing both alpha- and gamma-linked acidic amino acids were less efficiently hydrolyzed by PSMA but were most stable in plasma. Analogs were 5-10 fold more selectively toxic in vitro in the presence of active PSMA. These studies have identified PSMA selective, plasma stable peptide substrates that can be incorporated into prodrugs targeted for activation by PSMA within prostate cancer sites.

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ACCESSION NUMBER: 2004383856 EMBASE
TITLE: Genetic modification of T cells for cancer therapy.
AUTHOR: Imai C.; Campana D.
CORPORATE SOURCE: Dr. D. Campana, Department of Hematology-Oncology, St. Jude Children's Research Hosp., 332 North Lauderdale, Memphis, TN 38105-2794, United States. dario.campana@stjude.org
SOURCE: Journal of Biological Regulators and Homeostatic Agents, (2004) Vol. 18, No. 1, pp. 62-71. .
Refs: 109
ISSN: 0393-974X CODEN: JBRAER
COUNTRY: Italy
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
022 Human Genetics
030 Pharmacology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 24 Sep 2004
Last Updated on STN: 24 Sep 2004

AB The use of immune cells with restricted specificities for the treatment of cancer is a rapidly emerging area of clinical research. Chimeric receptors composed of the single-chain variable domain of murine antibodies and human signaling molecules are a promising tool to redirect the specificity of autologous or allogeneic immune cells. The success of this approach depends on the identification of target molecules expressed preferentially on cancer cells. Moreover, appropriate primary and secondary stimuli must be delivered to generate vigorous and durable immune responses. Since cancer cells often lack ligands for key co-stimulatory molecules, the addition of molecules such as CD28 or 4-1BB to the chimeric receptors can significantly improve their function. Studies in vitro and in animal models indicate that immune cells expressing chimeric receptors can have remarkable anti-cancer activity, while experimental and clinical data indicate that long-term persistence of adoptively transferred cells is feasible. Therefore, testing of this approach in clinical trials is warranted. We here review the principles and methodologies for designing chimeric receptors and delivering them into immune cells, as well as some of the potential complications associated with this form of cell therapy. .COPYRGT. Wichtig Editore, 2004.

L2 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:335142 CAPLUS
DOCUMENT NUMBER: 138:348687
TITLE: Use of selective tissue vascular thrombogens for

INVENTOR(S): targeting tumor tissues
 Liu, Cheng; Edgington, Thomas S.
 PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.; The
 Scripps Research Institute
 SOURCE: PCT Int. Appl., 100 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003035688	A2	20030501	WO 2002-EP11925	20021024
WO 2003035688	A3	20040318		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, UZ, VC, VN, YU, ZA, ZW RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
AU 2002350623	A1	20030506	AU 2002-350623	20021024
US 2003194400	A1	20031016	US 2002-279733	20021024
EP 1443954	A2	20040811	EP 2002-785305	20021024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRIORITY APPLN. INFO.:			US 2001-336331P	P 20011026
			US 2002-412194P	P 20020920
			WO 2002-EP11925	W 20021024

AB The invention provided compns. and methods to initiate site-specific thrombosis in tumor vasculature. The invention particularly provides Selective Tissue Vascular Thrombogens (STVTs) that can targeted thrombosis, infarction and destruction of selected tissues, for example, tumors. The present invention also provides methods for using the disclosed compns. and methods to treat tumors.

L2 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:334823 CAPLUS
 DOCUMENT NUMBER: 138:352761
 TITLE: Anti-prostate specific
 membrane antigen (PSMA) antibodies
 and fragments for cancer diagnosis and therapy and
 antitumor screening
 INVENTOR(S): Maddon, Paul J.; Donovan, Gerald P.; Olson, William C.; Schuelke, Norbert; Gardner, Jason; Ma, Dangshe
 PATENT ASSIGNEE(S): PSMA Development Company, L.L.C., USA
 SOURCE: PCT Int. Appl., 238 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003034903	A2	20030501	WO 2002-US33944	20021023
WO 2003034903	A3	20031030		
WO 2003034903	B1	20040513		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,				

UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2464239	AA	20030501	CA 2002-2464239	20021023
EP 1448588	A2	20040825	EP 2002-802198	20021023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005523683	T2	20050811	JP 2003-537481	20021023
US 2004033229	A1	20040219	US 2003-395894	20030321
US 2004161776	A1	20040819	US 2003-695667	20031027
US 2005215472	A1	20050929	US 2004-976352	20041027
PRIORITY APPLN. INFO.:				
			US 2001-335215P	P 20011023
			US 2002-362747P	P 20020307
			US 2002-412618P	P 20020920
			WO 2002-US33944	W 20021023
			US 2003-395894	A2 20030321
			US 2003-695667	A2 20031027

AB The invention includes antibodies or antigen-binding fragments thereof which bind specifically to conformational epitopes on the extracellular domain of PSMA, compns. containing one or a combination of such antibodies or antibodies or antigen-binding fragments thereof, hybridoma cell lines that produce the antibodies, and methods of using the antibodies or antigen-binding fragments thereof for cancer diagnosis and treatment. The invention also includes oligomeric forms of PSMA proteins, compns. comprising the multimers, and antibodies that selectively bind to the multimers.

L2 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:242117 CAPLUS
 DOCUMENT NUMBER: 138:276253
 TITLE: Methods and compositions for treating or preventing skin disorders using binding agents specific for prostate specific membrane antigen
 INVENTOR(S): Bander, Neil
 PATENT ASSIGNEE(S): Cornell Research Foundation, Inc., USA
 SOURCE: PCT Int. Appl., 225 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003024388	A2	20030327	WO 2002-US17204	20020530
WO 2003024388	A3	20030731		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2452288	AA	20030327	CA 2002-2452288	20020530
US 2003161832	A1	20030828	US 2002-160506	20020530
EP 1427377	A2	20040616	EP 2002-734612	20020530
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

JP 2005527474	T2	20050915	JP 2003-528486	20020530
PRIORITY APPLN. INFO.:			US 2001-324100P	P 20010920
			US 2002-362612P	P 20020308
			WO 2002-US17204	W 20020530

AB Methods and compns. for treating, preventing, or diagnosing epidermal or dermal disorders, e.g., psoriasis, are disclosed. The methods and compns. of the invention use binding agents, e.g., antibodies, specific for the extracellular domain of human prostate specific membrane antigen (PSMA).

L2 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:836381 CAPLUS
 DOCUMENT NUMBER: 139:341719
 TITLE: Use of bi-specific antibodies for pre-targeting diagnosis and therapy
 INVENTOR(S): Goldenberg, David M.; Hansen, Hans J.; Leung, Shui-on; McBride, William J.; Qu, Zhengxing
 PATENT ASSIGNEE(S): Immunomedics, Inc., USA
 SOURCE: U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of U.S. Ser. No. 823,746.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 17
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003198595	A1	20031023	US 2002-150654	20020517
US 7052872	B1	20060530	US 1999-382186	19990823
US 2002006379	A1	20020117	US 2001-823746	20010403
US 6962702	B2	20051108		
CA 2486307	AA	20031127	CA 2003-2486307	20030516
WO 2003097105	A1	20031127	WO 2003-GB2110	20030516
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003227939	A1	20031202	AU 2003-227939	20030516
EP 1506018	A1	20050216	EP 2003-725404	20030516
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003010088	A	20050405	BR 2003-10088	20030516
CN 1668335	A	20050914	CN 2003-816898	20030516
JP 2006506325	T2	20060223	JP 2004-505100	20030516
US 2005002945	A1	20050106	US 2004-776470	20040211
US 2006034759	A1	20060216	US 2005-198846	20050808
US 2006140858	A1	20060629	US 2005-514632	20050912
PRIORITY APPLN. INFO.:			US 1998-90142P	P 19980622
			US 1998-104156P	P 19981014
			US 1999-382186	A2 19990823
			US 2001-823746	A2 20010403
			US 1999-337756	A2 19990622
			US 2002-150654	A 20020517
			WO 2003-GB2110	W 20030516

AB The present invention relates to a bi-specific antibody or antibody fragment having at least one arm that specifically binds a targeted tissue and at least one other arm that specifically binds a targetable construct.

The targetable construct comprises a carrier portion which comprises or bears at least one epitope recognizable by at least one arm of said bi-specific antibody or antibody fragment. The targetable construct further comprises one or more therapeutic or diagnostic agents or enzymes. The invention provides constructs and methods for producing the bi-specific antibodies or antibody fragments, as well as methods for using them.

L2 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:449519 CAPLUS
DOCUMENT NUMBER: 137:28278
TITLE: Methods of treatment of angiogenesis-related disease involving human MDA-7 protein
INVENTOR(S): Chada, Sunil; Grimm, Elizabeth; Mhashilkar, Abner; Schrock, Bob; Rajagopal, Ramesh
PATENT ASSIGNEE(S): University of Texas, USA
SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002045737	A2	20020613	WO 2001-US47215	20011207
WO 2002045737	A3	20040108		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2429769	AA	20020613	CA 2001-2429769	20011207
AU 2002020257	A5	20020618	AU 2002-20257	20011207
US 2002183271	A1	20021205	US 2001-17472	20011207
EP 1404359	A2	20040407	EP 2001-999382	20011207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005500247	T2	20050106	JP 2002-547520	20011207
PRIORITY APPLN. INFO.:			US 2000-254226P	P 20001207
			WO 2001-US47215	W 20011207

AB The invention relates to gene therapy methods for the treatment of human disease. More specifically, the invention is directed to methods for treating a subject with an angiogenesis-related disease. In one embodiment, an adenoviral expression construct comprising a nucleic acid encoding a human MDA-7 protein under the control of a promoter operable in eukaryotic cells, is administered to said patient with a angiogenesis-related disease. The present invention thus provides for treatment of angiogenesis-related disease by through expression of mda-7 and inhibition angiogenesis. Such diseases include cancer.

L2 ANSWER 20 OF 24 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:404358 BIOSIS
DOCUMENT NUMBER: PREV200100404358
TITLE: Hydrolysis of methotrexate analogs by prostate-specific membrane antigen (PSMA).
AUTHOR(S): Gady, Alyssa M. [Reprint author]; Rosen, D. Marc; Denmeade,

Samuel R.
CORPORATE SOURCE: The Johns Hopkins School of Medicine, Baltimore, MD, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 230. print.
Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research. New Orleans, LA, USA.
March 24-28, 2001. American Association for Cancer Research.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Aug 2001
Last Updated on STN: 22 Feb 2002

L2 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:144870 CAPLUS
TITLE: Synthesis of N-thiophosphonyl derivatives of glutamic acid
AUTHOR(S): Dastgah, Azar; Lu, Haiyan; Mlodnosky, Karyn L.; Dinh, Trang T.; Berkman, Clifford E.
CORPORATE SOURCE: Dept. of Chemistry & Biochemistry, San Francisco State Univ., San Francisco, CA, 94132, USA
SOURCE: Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., March 21-25 (1999), CHED-397. American Chemical Society: Washington, D. C.
CODEN: 67GHA6
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB Recently, it has been noted that increased intra- and extra-cellular levels of folate hydrolyzing enzymes (Gamma-Glutamyl Hydrolase, GGH; prostate specific membrane antigen, PSM) are associated with tumor cell resistance to the antiproliferative drug methotrexate (MTX). Therefore, inhibitors of GGH or PSM could be therapeutically invaluable for combating MTX-resistant tumors by countering their mode of resistance. Initial studies indicated that traditional, phosphonamide tetrahedral-intermediate analog inhibitors were unsuccessful against the target hydrolases. However, recent preliminary data has shown that the corresponding thiophosphonamide analogs exhibit inhibitory activity against PSM and GGH. The synthesis of a limited series of these N-thiophosphonyl derivs. of glutamic acid will be presented.

L2 ANSWER 22 OF 24 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 97330810 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9187245
TITLE: Structure of membrane glutamate carboxypeptidase.
AUTHOR: Rawlings N D; Barrett A J
CORPORATE SOURCE: Department of Immunology, The Babraham Institute, Cambridge, UK.
SOURCE: Biochimica et biophysica acta, (1997 May 23) Vol. 1339, No. 2, pp. 247-52.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 16 Jul 1997
Last Updated on STN: 3 Mar 2000
Entered Medline: 1 Jul 1997
AB Membrane glutamate carboxypeptidase (mGCP) hydrolyses pteroylpoly-gamma-glutamates, methotrexate tri-gamma-glutamate and N-acetyl-aspartyl-alpha-glutamate. The enzyme is thought to be required

for intestinal uptake of folate, for the resistance of some tumours to methotrexate, and for the metabolism of N-acetyl-aspartyl-glutamate, an abundant neuropeptide. It has recently been reported that mGCP is a protein also known as prostate-specific membrane antigen, homologous with transferrin receptor. This allows us to predict the domain structure of mGCP. Moreover, we have been able to assign the catalytic domain of mGCP to peptidase family M28, which contains cocatalytic zinc metallopeptidases. On the basis of the known structure of an aminopeptidase in family M28, we predict that Asp377, Asp387, Glu425, Asp453 and His553 are ligands of two atoms of zinc bound in the catalytic site of mGCP, and suggest that the aminopeptidases of *Vibrio* and *Streptomyces* can serve as valuable models in the design of inhibitors for this medically important enzyme.

L2 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:738993 CAPLUS

DOCUMENT NUMBER: 128:21580

TITLE: Prostate-specific membrane

antigen, a unique folate hydrolase: potential target for prodrug therapy

AUTHOR(S): Heston, Warren D. W.; Tong, W. P.; Pinto, J. T.

CORPORATE SOURCE: Urologic Oncology Research Laboratory, Molecular Pharmacology and Experimental Therapeutics Section, Sloan-Kettering Institute for Cancer Research, New York, NY, USA

SOURCE: Molecular Urology (1997), 1(2/3), 215-219

CODEN: MOURFE; ISSN: 1091-5362

PUBLISHER: Liebert

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The aim of the current investigation was to determine whether prostate-specific membrane (PSM) antigen can be used as a prodrug target. In searching to identify the function of PSM antigen, we observed that it is a unique carboxypeptidase, which has hydrolytic activity with carboxy-terminal peptidic bonds involving glutamate. It is unique in that it will hydrolyze gamma- and alpha-linked peptides, such as the alpha linkage in N-acetylaspartylglutamate and the gamma-linked glutamates in polygammaglutamated folate or methotrexate. A substrate used to study the activity of PSM antigen is methotrexate trigammaglutamate. Because the trigammaglutamate is a poor substrate for transportation into the cell, we examined it as a potential prodrug form of this traditional anticancer drug. When we incubated it with LNCaP tumor cells, it was cytotoxic. We then incubated it with PC-3 cells that were or were not transfected with PSM antigen and found that it was cytotoxic to the PSM antigen-expressing cells. Polygammaglutamated folate antagonists should be considered for therapeutic approaches in prostate cancer.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 24 OF 24 MEDLINE on STN

DUPLICATE 4

ACCESSION NUMBER: 1999035167 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9816319

TITLE: Prostate-specific membrane

antigen: a novel folate hydrolase in human prostatic carcinoma cells.

AUTHOR: Pinto J T; Suffoletto B P; Berzin T M; Qiao C H; Lin S; Tong W P; May F; Mukherjee B; Heston W D

CORPORATE SOURCE: Nutrition Research Laboratory, Urology Research Laboratory, Pharmacology Analytical Laboratory, and George M. O'Brien Urology Research Center, Memorial Sloan-Kettering Cancer Center, New York, New York 10021, USA.

CONTRACT NUMBER: CA 08748-29 (NCI)

CA 39203 (NCI)

DK/CA 47650 (NIDDK)

+

SOURCE: Clinical cancer research : an official journal of the American Association for Cancer Research, (1996 Sep) Vol. 2, No. 9, pp. 1445-51.
Journal code: 9502500. ISSN: 1078-0432.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199902

ENTRY DATE: Entered STN: 11 Mar 1999
Last Updated on STN: 3 Mar 2000
Entered Medline: 25 Feb 1999

AB A novel monoclonal antibody has been developed that reacts strongly with human prostatic cancer, especially tumors of high grade. This antibody (7E11C-5) is currently in Phase 3 trials as an imaging agent for metastatic disease. We have cloned the gene that encodes the antigen that is recognized by the 7E11C-5 monoclonal antibody and have designated this unique protein prostate-specific membrane (PSM) antigen. PSM antigen is a putative class II transmembranous glycoprotein exhibiting a molecular size of Mr 94,000. Functionally, class II membrane proteins serve as transport or binding proteins or have hydrolytic activity. Preliminary studies have demonstrated binding of pteroylmonoglutamate (folate) to membrane fractions that also cross-reacted with the PSM monoclonal antibody. We observed substantial carboxypeptidase activity as folate hydrolase associated with PSM antigen. The purpose of our study was to demonstrate that human prostatic carcinoma cells expressing PSM antigen exhibit folate hydrolase activity using methotrexate triglutamate (MTXGlu3) and pteroylpentaglutamate (PteGlu5) as substrates. Isolated membrane fractions from four human prostate cancer cell lines (LNCaP, PC-3, TSU-Pr1, and Duke-145) were examined for folate hydrolase activity using capillary electrophoresis. After timed incubations at various pH ranges and in the presence and absence of thiol reagents, separation of pteroyl(glutamate)_n derivatives was achieved with an electrolyte of sodium borate and SDS, while absorbance was monitored at 300 nm. The results demonstrate clearly that LNCaP cells, which highly express PSM, hydrolyze gamma-glutamyl linkages of MTXGlu3. The membrane-bound enzyme is an exopeptidase, because it progressively liberates glutamates from MTXGlu3 and PteGlu5 with accumulation of MTX and PteGlu1, respectively. The semipurified enzyme has a broad activity from pH 2.5 to 9.5 and exhibits activity maxima at pH 5 and 8. Enzymatic activity is maintained in the presence of reduced glutathione, homocysteine, and p-hydroxymercuribenzoate (0.05-0.5 mm) but was inhibited weakly by DTT (>/=0.2 mm). By contrast to LNCaP cell membranes, membranes isolated from other human prostate adenocarcinoma cells (PC-3, Duke-145, and TSU-Pr1) did not exhibit comparable hydrolase activity, nor did they react with 7E11-C5 monoclonal antibody. After transfection of PC-3 cells with a full-length 2.65-kb PSM cDNA subcloned into a pREP7 eukaryotic expression vector, non-PSM antigen-expressing PC-3 cells developed immunoreactivity to 7E11-C5 monoclonal antibody and demonstrated folate hydrolase activities and optimum pH activity profiles identical to those of LNCaP cells. The membrane-bound enzymes from both LNCaP- and PC-3-transfected cells also have a capacity to hydrolyze an alpha-linked glutamyl moiety from N-acetyl-alpha-aspartylglutamate. We have identified that PSM antigen is a pteroyl poly-gamma-glutamyl carboxypeptidase (folate hydrolase) and is expressed strongly in human prostate cancer. Cancer cells that express this enzyme are resistant to methotrexate therapy. Those developing future therapeutic strategies in the treatment of prostate cancer that utilize folate antagonists need to consider this mechanism of resistance.

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NEWS 10 JUN 26 TULSA/TULSA2 reloaded and enhanced with new search and
and display fields
NEWS 11 JUN 28 Price changes in full-text patent databases EPFULL and PCTFULL
NEWS 12 JUL 11 CHEMSAFE reloaded and enhanced
NEWS 13 JUL 14 FSTA enhanced with Japanese patents
NEWS 14 JUL 19 Coverage of Research Disclosure reinstated in DWPI
NEWS 15 AUG 09 INSPEC enhanced with 1898-1968 archive
NEWS 16 AUG 28 ADISCTI Reloaded and Enhanced
NEWS 17 AUG 30 CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 18 SEP 11 CA/CAplus enhanced with more pre-1907 records
NEWS 19 SEP 21 CA/CAplus fields enhanced with simultaneous left and right
truncation
NEWS 20 SEP 25 CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS 21 SEP 25 CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 22 SEP 25 CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 23 SEP 28 CEABA-VTB classification code fields reloaded with new
classification scheme

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L2 ANSWER 1 OF 2 MEDLINE on STN

ACCESSION NUMBER: 2001510071 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11557259

TITLE: Binding of the glutamate carboxypeptidase II (NAALADase) inhibitor 2-PMPA to rat brain membranes.

AUTHOR: Tiffany C W; Cai N S; Rojas C; Slusher B S

CORPORATE SOURCE: Guilford Pharmaceuticals Inc., 6611 Tributary Street, Baltimore, MD 21224, USA.

SOURCE: European journal of pharmacology, (2001 Sep 14) Vol. 427, No. 2, pp. 91-6.

Journal code: 1254354. ISSN: 0014-2999.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200111

ENTRY DATE: Entered STN: 17 Sep 2001

Last Updated on STN: 5 Nov 2001

Entered Medline: 1 Nov 2001

AB 2-Phosphonomethyl pentanedioic acid (2-PMPA) is a potent and selective inhibitor of glutamate carboxypeptidase II (NAALADase), and has shown robust neuroprotective activity in both in vitro and in vivo models of ischemia. In the brain, glutamate carboxypeptidase II (GCPII) (EC3.4.17.21) hydrolyzes the neuropeptide N-acetylaspartylglutamate (NAAG) to glutamate and N-acetylaspartate. We report the development and characterization of a [(3)H]2-PMPA binding assay. [(3)H]2-PMPA binding was dependent on protein concentration, saturable, and displaceable. The association ($k_{(on)}$) and dissociation ($k_{(off)}$) rate constants were $3 \times 10(6)$ M (-1) s (-1) and 0.01 s (-1) , respectively. The dissociation equilibrium constant (K_d) determined from the ratio of the rate constants ($K_d = k_{(off)} / k_{(on)}$) was 1 nM. Scatchard analysis revealed one binding site with $K_d = 2$ nM and $B_{(max)} = 0.7$ pmol/mg. Binding exhibited similar pharmacological properties to GCPII enzyme activity, including chloride dependency, cobalt stimulation and inhibition by phosphate and

quisqualate. The binding of [³H]2-PMPA also showed tissue specificity in that tissues previously reported to be devoid of GCPII enzymatic activity were devoid of [³H]2-PMPA binding. [³H]2-PMPA binding represents an additional probe for the study of GCPII activity, and may be useful as a high throughput screening assay.

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| L2 ANSWER 2 OF 2 | MEDLINE on STN | DUPLICATE 1 |
| ACCESSION NUMBER: | 1998041505 MEDLINE | |
| DOCUMENT NUMBER: | PubMed ID: 9375657 | |
| TITLE: | Molecular cloning of a peptidase against N-acetylaspartylglutamate from a rat hippocampal cDNA library. | |
| AUTHOR: | Bzdega T; Turi T; Wroblewska B; She D; Chung H S; Kim H; Neale J H | |
| CORPORATE SOURCE: | Department of Biology, Georgetown University, Washington, D.C. 20057-1229, U.S.A. | |
| SOURCE: | Journal of neurochemistry, (1997 Dec) Vol. 69, No. 6, pp. 2270-7.
Journal code: 2985190R. ISSN: 0022-3042. | |
| PUB. COUNTRY: | United States | |
| DOCUMENT TYPE: | Journal; Article; (JOURNAL ARTICLE) | |
| LANGUAGE: | English | |
| FILE SEGMENT: | Priority Journals | |
| OTHER SOURCE: | GENBANK-U75973 | |
| ENTRY MONTH: | 199712 | |
| ENTRY DATE: | Entered STN: 9 Jan 1998
Last Updated on STN: 3 Mar 2000
Entered Medline: 12 Dec 1997 | |
| AB | N-Acetylaspartylglutamate (NAAG) is the most prevalent peptide neurotransmitter in the mammalian nervous system. NAAG selectively activates the type 3 metabotropic glutamate receptor. It is inactivated by peptidase activity on the extracellular face of the plasma membrane of neurons and glia. The human gene that codes for prostate -specific membrane antigen (PSM) has been shown to produce peptidase activity against NAAG. We cloned the human PSM cDNA and used it to probe a rat hippocampal cDNA library. We identified a cDNA containing a complete coding region that possesses 83% homology with the PSM gene. The predicted 752-amino acid sequence has 85% identity and 91% similarity to the PSM sequence. CHO cells transfected with this cDNA expressed NAAG peptidase activity at a level similar to that obtained from rat brain membranes. The peptidase activity was inhibited by beta-NAAG, quisqualate, and pteroylglutamate but not aspartylglutamate or pteroic acid. In situ hybridization data demonstrated the widespread distribution of the peptidase mRNA in the brain, consistent with the distribution of peptidase activity. The highest levels of hybridization were detected in the hippocampus, dentate gyrus, piriform cortex, choroid plexus of the ventricles, pineal gland, anterior pituitary, and supraoptic nucleus. Three transcripts (estimated at 5, 3.4, and 2.9 kb) were identified in northern blots of rat brain, while in rat kidney the third transcript appeared slightly smaller than 2.9 kb. With use of reverse transcriptase PCR with primers for the 5' end, the central region, and the 3' end of the hippocampal cDNA, the expected amplification products were obtained from rat brain RNA. Spinal cord yielded an amplification product only with primers for the 5' end of the hippocampal cDNA. | |

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NEWS 11 JUN 28 Price changes in full-text patent databases EPFULL and PCTFULL
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NEWS 13 JUL 14 FSTA enhanced with Japanese patents
NEWS 14 JUL 19 Coverage of Research Disclosure reinstated in DWPI
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NEWS 22 SEP 25 CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 23 SEP 28 CEABA-VTB classification code fields reloaded with new classification scheme

NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

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L2 ANSWER 1 OF 2 MEDLINE on STN

DUPLICATE 1

ACCESSION NUMBER: 1998041505 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9375657

TITLE: Molecular cloning of a peptidase against
N-acetylaspartylglutamate from a rat hippocampal cDNA
library.

AUTHOR: Bzdega T; Turi T; Wroblewska B; She D; Chung H S; Kim H;
Neale J H

CORPORATE SOURCE: Department of Biology, Georgetown University, Washington,
D.C. 20057-1229, U.S.A.

SOURCE: Journal of neurochemistry, (1997 Dec) Vol. 69, No. 6, pp.
2270-7.

Journal code: 2985190R. ISSN: 0022-3042.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-U75973

ENTRY MONTH: 199712

ENTRY DATE: Entered STN: 9 Jan 1998

Last Updated on STN: 3 Mar 2000

Entered Medline: 12 Dec 1997

AB N-Acetylaspartylglutamate (NAAG) is the most prevalent peptide neurotransmitter in the mammalian nervous system. NAAG selectively activates the type 3 metabotropic glutamate receptor. It is inactivated by peptidase activity on the extracellular face of the plasma membrane of neurons and glia. The human gene that codes for prostate -specific membrane antigen (PSM) has been shown to produce peptidase activity against NAAG. We cloned the human PSM cDNA and used it to probe a rat hippocampal cDNA library. We identified a cDNA containing a complete coding region that possesses 83% homology with the PSM gene. The predicted 752-amino acid sequence has 85% identity and 91% similarity to the PSM sequence. CHO cells transfected with this cDNA expressed NAAG

peptidase activity at a level similar to that obtained from rat brain membranes. The peptidase activity was inhibited by beta-NAAG, quisqualate, and pteroylglutamate but not aspartylglutamate or pteroic acid. In situ hybridization data demonstrated the widespread distribution of the peptidase mRNA in the brain, consistent with the distribution of peptidase activity. The highest levels of hybridization were detected in the hippocampus, dentate gyrus, piriform cortex, choroid plexus of the ventricles, pineal gland, anterior pituitary, and supraoptic nucleus. Three transcripts (estimated at 5, 3.4, and 2.9 kb) were identified in northern blots of rat brain, while in rat kidney the third transcript appeared slightly smaller than 2.9 kb. With use of reverse transcriptase PCR with primers for the 5' end, the central region, and the 3' end of the hippocampal cDNA, the expected amplification products were obtained from rat brain RNA. Spinal cord yielded an amplification product only with primers for the 5' end of the hippocampal cDNA.

L2 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 96149377 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8570628
TITLE: Prostate-specific membrane antigen is a hydrolase with substrate and pharmacologic characteristics of a neuropeptidase.
AUTHOR: Carter R E; Feldman A R; Coyle J T
CORPORATE SOURCE: Department of Psychiatry, Massachusetts General Hospital-East, Charlestown 02129, USA.
CONTRACT NUMBER: MH-572901 (NIMH)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1996 Jan 23) Vol. 93, No. 2, pp. 749-53.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF039707
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 15 Mar 1996
Last Updated on STN: 3 Mar 2000
Entered Medline: 1 Mar 1996

AB This report demonstrates that the investigational prostatic carcinoma marker known as the prostate-specific membrane antigen (PSM) possesses hydrolytic activity with the substrate and pharmacologic properties of the N-acetylated alpha-linked acidic dipeptidase (NAALADase). NAALADase is a membrane hydrolase that has been characterized in the mammalian nervous system on the basis of its catabolism of the neuropeptide N-acetylaspartylglutamate (NAAG) to yield glutamate and N-acetylaspartate and that has been hypothesized to influence glutamatergic signaling processes. The immunoscreening of a rat brain cDNA expression library with anti-NAALADase antisera identified a 1428-base partial cDNA that shares 86% sequence identity with 1428 bases of the human PSM cDNA [Israeli, R. S., Powell, C. T., Fair, W. R. & Heston, W.D.W. (1993) Cancer Res. 53, 227-230]. A cDNA containing the entire PSM open reading frame was subsequently isolated by reverse transcription-PCR from the PSM-positive prostate carcinoma cell line LNCaP.. Transient transfection of this cDNA into two NAALADase-negative cell lines conferred NAAG-hydrolyzing activity that was inhibited by the NAALADase inhibitors quisqualic acid and beta-NAAG. Thus we demonstrate a PSM-encoded function and identify a NAALADase-encoding cDNA. Northern analyses identify at least six transcripts that are variably expressed in NAALADase-positive but not in NAALADase-negative rat tissues and human cell lines; therefore, PSM and/or related molecular species appear to account for NAAG hydrolysis in the nervous system. These results also raise questions about the role of PSM in both normal and pathologic prostate epithelial-cell function.

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